SYNTHESIS AND BIOLOGICAL ACTIVITY STUDIES OF ARYLHYDRAZONES AND HETEROCYCLIC COMPOUNDS

SYNOPSIS

OF THE Ph.D. THESIS TO BE SUBMITTED TO THE

MANGALORE UNIVERSITY

FOR THE AWARD OF THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN

CHEMISTRY

By

Mrs. Rajatha M

DEPARTMENT OF CHEMISTRY
MANGALORE UNIVERSITY
MANGALAGANGOTHRI-574 199
KARNATAKA, INDIA.

SEPTEMBER-2024

SYNOPSIS OF THE THESIS TO BE SUBMITTED TO THE MANGALORE UNIVERSITY

FOR THE AWARD OF THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY

Title of the Thesis : **Synthesis and Biological Activity Studies of Arylhydrazones and Heterocyclic Compounds**

Name of the Candidate : **Mrs. Rajatha M**

Name of the Guide : **Prof. Jagadeesh Prasad D**

Date of Registration : **01-03-2017**

Registration : **MU/EXB/Ph.D./CR.197/Chem./2018-19/E.13, Dated 23.02.2019**

Place of Work : **Department of Chemistry**
Mangalore University
Mangalagangothri-574 199
Karnataka, India.

SYNTHESIS AND BIOLOGICAL ACTIVITY STUDIES OF ARYLHYDRAZONES AND HETEROCYCLIC COMPOUNDS

Heterocyclic compounds are the most important class of organic compounds in which nitrogen, sulphur and oxygen bearing compounds are most prominent one[1]. Most of the naturally occurring compounds are containing heterocyclic ring in which pyrimidine and purine rings are basis for genetic material DNA. Some of the heterocyclic compounds used in medicine includes amino acids like proline, histidine and tryptophan, the vitamins and co-enzyme precursors such as thiamine, riboflavin, pyridoxine, folic acid, biotin, B_{12} and E[2]. Heterocyclic compounds with great physical and chemical properties extends their activity in many fields beyond pharmaceuticals[3].

Five member heterocyclic compounds such as pyrrole, pyrazole, imidazole, furan, thiazole, triazoles and their benzo derivatives with excess of pi-electrons finds numerous application in the field of medicinal chemistry[4]. Theyexhibit antifungal[5], antibacterial[6], antiproliferrative[7], antidiabetic[8], anticancer[9], anti-inflammatory[10], antioxidant[11], antitubercular[12], antimalarial[13], antiviral[14], HIV-1[15], anticonvulsant[16] activity. Further these compounds find application as fluorescent chemosensors[17], anticorrosive[18], transistors[19] and fluorescent dyes[20].

Six member heterocyclic compounds are also important scaffolds as they exhibit biological activities such as antimicrobial[21], anti-inflammatory[22], anticancer[23], anti-diabetic[24], antiviral[25], anticonvulsant and antiparkinson[26], antitubercular[27], antimalarial[28], anti HIV[29]. Apart from this, they are also used in solar cells[30], light emitting diodes[31], dyes[32], fluorosence sensor[33] etc.

Hence, this thesis reflects on synthesis, characterization and biological activities of the simple & fused heterocyclic compounds.

The thesis has been divided into five chapters.

CHAPTER I: Synthesis, Crystallography and Biological Activity Studies of Some Hydrazone Derivatives of 4-methoxybenzohydrazide

Hydrazones are compounds with inter linked nitrogen atoms[34]. Due to the presence of azomethine group, derivatives of these compounds found its wide utilization in organic synthesis[35]. The presence of C=N-NH group exhibits nucleophilic imine and amino type of nitrogen, imine carbon bearing nucleophilic and electrophilic character, acidic N-H proton and configurational isomerism made this as one of the lead compound in the field of science and technology[36]. Hydrazones were reported to possess numerous biological activities like anti-inflammatory[37,38], antiulcer[39], larvicidal[40], antibacterial[41], antifungal[42], antianalgesic[43], antioxidant[44], anticancer[45], antimicrobial[46,47], enzyme inhibitor[48], antiproliferative and apoptosis induction potential activity[49], mammalian cathepsin B and cathepsin H inhibitors[50].Prompted by these findings, we synthesized some hydrazone derivatives of 4-methoxy benzohydrazide derivatives and screened for their biological activities.

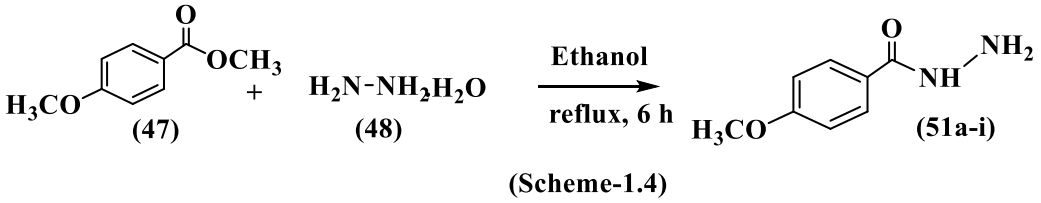
Materials and Methods

The intermediate 4-methoxybenzhydrazide **(49)** was prepared according to the procedure reported in the literature[51]. To a stirred solution of 4-methoxy-methylbenzoate **(47)** (0.03 mol) in ethanol, hydrazine hydrate **(48)** (0.150 mol) was added dropwise and refluxed for 6h. The completion of the reaction was monitored by thin layer chromatography (TLC).After completion of the reaction, solvent was evaporated and solid separated was collected **(49)**.

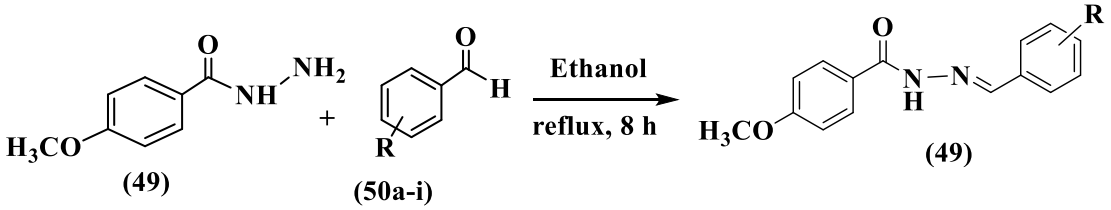
Further targeted (*E*)-*N*'-benzylidene-4-methoxy benzohydrazide derivatives[52,53]**(51a-i)** were obtained by refluxing **e**quimolar quantities of 4-methoxybenzohydrazide **(49)** (0.004 mol) and various substituted benzaldehyde **(50a-i)**(0.004 mol) in presence of ethanol. After completion of the reaction, reaction mixture was cooled and product separated was filtered, washed and dried. The recrystallization was done using ethanol. The reactions are outlined in Scheme 1.

Newly synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, FT-IR and Mass spectral studies. All compounds were screened for antimicrobial, anticancer activities and nonlinear optics were determined by second order harmonic generation assay. One of the compounds (**51g**) was studied for inter and intramolecular interactions by single crystal X-ray method.

Reaction Scheme



(Scheme-1.4)



(Scheme-1.5)

R=4-Cl-3-NO_2; 3-Br-4-F; 2,4-Cl_2; 3,4-$(OCH_3)_2$-6-NO_2; 6-Br-(3,4-$OCH_3)_2$; 2-Cl-5-CF_3; 4-OH-3,5-$(OCH_3)_2$; 4-OCH_3-3-NO_2; 3-Br-4-OCH_3

CHAPTER II: Synthesis, Crystallography, Computational and Biological Activity Studies of Novel Thiadiazolopyrimidine Derivatives

Multicomponent reactions (MCRs) are major tools that adheres to the principles of green chemistry[54]. Due to embedded hetero atoms in the ring system, heterocyclic compounds have attracted scientific community to explore further for novel therapeutic agents. In the current investigation we designed and synthesized thiadiazolopyrimidine motifs by one pot MCR. Since thiadiazole containing structural scaffold serves as a “two electron donor system” and are well

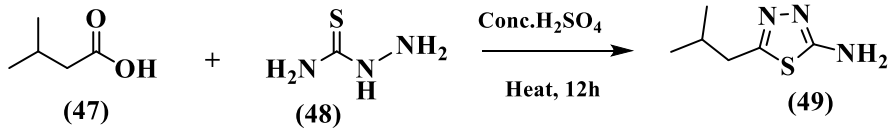
known as “hydrogen bonding domain” finds application in medicinal, agricultural, and materials chemistry[55]. Thiadiazole containing structural motifs acts as antimicrobial[56], anti-inflamatory[57], anticancer[58], antidiabetic[59] agents. They also finds application in corrosion inhibition[60], optoelectonics[61]. Pyrimidine is the six member azaheterocycle with potential application in medicine as well as applied chemistry[62]. Pyrimidine embedded compounds core motifs were well reported as antibacterial[63], antidiabetic[64], anticancer[23], anticonvulsant[65], anti-inflammatory[22], antiviral[25],dye-sensitized solar cells[66], fluorosence sensor[33]. Thiadiazolopyrimidine derivatives having bridgehead nitrogen atom are present in number of natural as well as synthetic compounds and are effective as herbicidal[67], antitumor[68], antimicrobial[69]agents.

Considering the pharmacological significance of bridgehead heterocycles, we synthesized novel thiadiazolopyrimidine derivatives and to explored for various biological activities.

Materials and Method

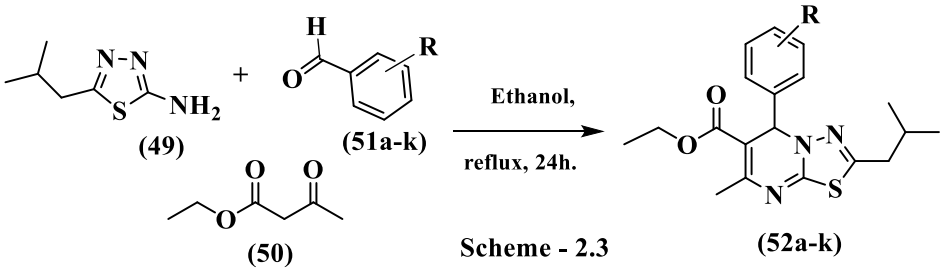
The 5-isobutyl-1,3,4-thiadiazol-2-amine **(49)** was prepared as mentioned in the literature[70]. An equimolar mixture of isovaleric acid **(47)** (0.0018 mol) and thiosemicarbazide **(48)** (0.0051 mol) were heated in presence of Conc.H_2SO_4 for 12 h. The reaction mixture was gently basified using ammonia. The white solid formed was filtered by washing with water, collected, dried and used for further step after recrystallization with ethanol.

Reaction Scheme



(47) (48) (49)

Scheme - 2.2



(49) (51a-k) (50) (52a-k)

Scheme - 2.3

R = 2,4-Cl_2; 2,4-$(OCH_3)_2$; 4-Cl; 2-OCH_3-5-Br; 4-Br; 4-NO_2; 3-NO_2-4-Cl; 2-Cl-5-NO_2; 3-Br-4-OCH_3; 2-Cl-4-F; 2-Cl-5-CF_3

In order to synthesize ethyl-2-isobutyl-7-methyl-5-(substitutedphenyl)-5*H*-[1,3,4]thiadiazolo[3,2-*a*]pyrimidine-6-carboxylate drivatives **(52a-k)**, a mixture of 5-isobutyl-1,3,4-thiadiazol-2-amine **(49)** (0.0032 mol), substituted benzaldehydes (**51a-k)** (0.0032 mol) and ethyl acetoacetate **(50)** (0.0032 mol) were taken in a round bottom flask. The contents were refluxed for about 24 h., in an oil bath in presence of ethanol as solvent. Completion of the reaction was monitored by TLC at regular intervals (EtOAc:hexane 2:8) and poured to crushed ice. The column chromatography was

used to get pure product[71,72]. All the synthesized compounds were characterized by ^{1}H-NMR, ^{13}C-NMR and Mass spectral studies. Synthesized compounds were screened for their antimicrobial, antioxidant, and anti-inflammatory activities. Further compound **(52h)** was subjected to computational and Crystal parameters of the compounds (**52f)** and (**52h)** were determined.

CHAPTER III: Synthesis and Biological Activity Studies of Novel Imidazothiadiazole Derivatives

1,3,4-thiadiazole and their derivatives possess excellent biological activity[73]. Imidazoles are the polar, planar five member ring systems with 3C and 2N incorporated in numerous biomolecules including histidine. Imidazole embedded structural motifs finds application in medicine as well as in other fields such as corrosion inhibitors, fire retardant, photography and electronics[74,75]. Two or more pharmacophores united forms hybrid compounds and exhibits wide spectrum of pharmaceutical activities[76]. Imidazothiadiazoles are also potential as antifungal[77], antimicrobial[78,79], anti-inflamatory[80], anticancer[81–83], antileukemic[84], human carbonic anhydrase IX and XII inhibitors[85], antihyperlipidemic[86] agents.

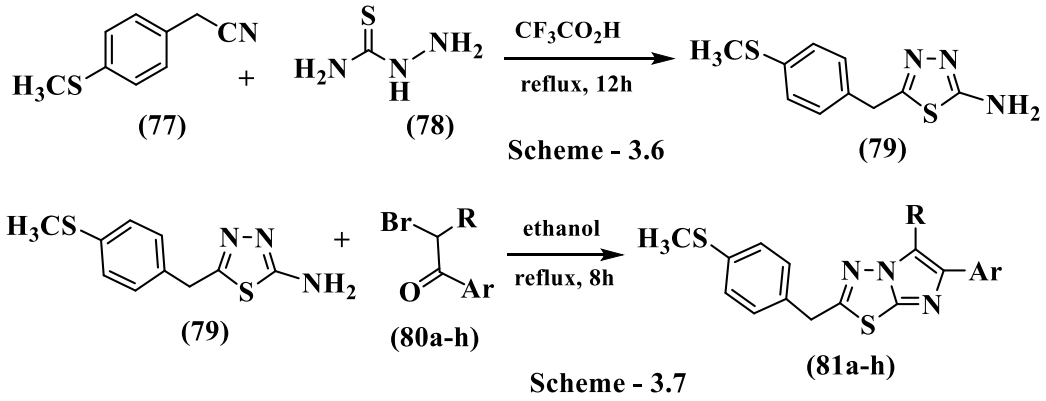
Hence keeping biological significance of imidazole and thiadiazole derivatives in mind, we synthesized novel imidazothiadiazole derivatives and investigated their biological activities.

Materials and Method

The intermediate 5-(4-(methylthio)benzyl)-1,3,4-thiadiazol-2-amine **(79)** was prepared according to the reported literature[87]. To a round bottom flask containing a mixture of 2-(4-(methylthio)phenyl)acetonitrile **(77)** (0.0018 mol) and thiosemicarbazide **(78)** (0.0051 mol), added 30 mL of trifluoroacetic acid and refluxed at 75 ℃ for 12h. The completion of the reaction was monitored by thin layer chromatography. After completion of the reaction, the reaction mixture was neutralized with ammonia solution. The white solid formed was collected by filtration and washed, recrystallized from ethanol.

A mixture of 5-(4-(methylthio)benzyl)-1,3,4-thiadiazol-2-amine **(79)** (0.0021 mol) and substituted phenacyl bromides **(80a-h)**(0.0021 mol) were dissolved in ethanol and refluxed for 8 h. After completion of the reaction, (monitored by TLC) excess of solvent was distilled off. The solid formed **(81a-h)** was collected, washed with water, dried and recrystallized from ethanol and DMF mixture[88]. The compounds obtained were confirmed by various spectroscopic techniques like ^{1}H-NMR, ^{13}C-NMR and Mass spectral studies. All the synthesized compounds were screened for their antioxidant and anti-inflammatory activity.

Reaction Scheme



Ar = biphenyl, R = H; Ar = 3,4-$(Cl)_2$-Ph, R = H; Ar = Ph, R = CH_3; Ar = 4-CF_3-Ph, R = H; Ar = naphthalene, R = H; Ar = 4-OH-3-$CONH_2$-Ph, R = H; Ar = 2,4-$(Cl)_2$-Ph, R = H; Ar = 3-NO_2-Ph, R = H

CHAPTER IV: Synthesis and Biological Activity Studies of Novel Thiazolidin-4-one Derivatives

Thiazolidine-4-one derivatives emerged as persuasive motifs with their wide spread pharmacological applications. For instance, penicillin is one of the privileged scaffold containing thiazolidine moiety which serves as important antibiotic worldwide[89]. Thiazolidinone compounds were found to possess anticancer[90,91], antianalgesic and anti-inflammatory[92], anticonvulsant[16,93], HIV-1 RT inhibitors[94,95], protein tyrosinephosphate-1B inhibitors[96], antidiabetic[8,97], antibiofilm[98], antioxidant[99,100], antitumor[101], cyclooxygenase inhibitor[102], human mitotic kinesin Eg5 inhibitor[103], antiviral[104], antihistaminic[105], dye[106], antitoxoplasma gondii[107], fluorescent chemosensors[17], antituberculor[108], anti-corrosive[18], antihyperglycaemic and antidyslipidemic[109], anti-hypertensive[110].Hence attracted by the biological importance of thiazolidinone compounds, we synthesized novel thiazolidinone derivatives and screened them for biological activities.

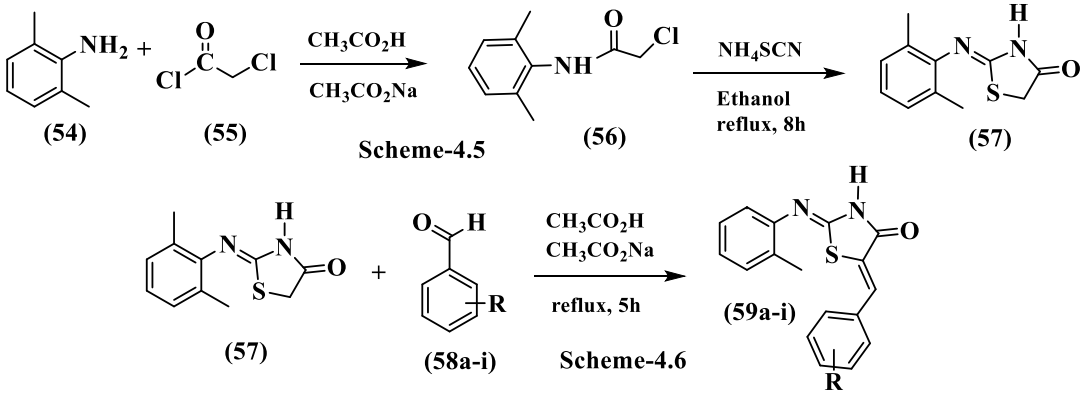
Materials and Method

In the first step 2-chloro-N-(2,6-dimethyl)acetamide **(56)** was prepared as mentioned in the literature[111]. To a stirred solution of 2,6-dimethylaniline **(54)**(0.01 mol) in 15 mL of glacial acetic acid added choloroacetyl chloride **(55)** (0.01 mol) and 25 mL of aqueous saturated solution of sodium acetate. The product formed **(56)** was stirred thoroughly with cold water and filtered.

Further 2-((2,6-dimethylphenyl)imino)thiazolidin-4-one **(57)** was synthesized according to the literature[112]. A mixture 2-chloro-N-(2,6-dimethyl)acetamide**(56)** (0.013 mol) and ammonium acetate (0.015 mol) were refluxed in presence of ethanol for 5 h. After completion of the reaction (monitored by TLC), reaction mixture was poured into ice-cold water and solid formed **(57)** was collected by filtration.

A mixture of 2-((2,6-dimethylphenyl)imino)thiazolidin-4-one **(57)**(0.0014 mol) and various substituted benzaldehydes **(58a-j)**(0.0014 mol) were refluxed for about 5 h in presence of acetic acid, which was buffered with sodium acetate. The solid formed **(59a-i)** was separated, washed with water dried and recrystallized from acetic acid-DMF solvent system[112]. Reaction scheme is given in Scheme 4.0. Newly synthesized compounds were characterized by ^{1}HNMR, ^{13}C NMR and Mass spectral data. All compounds were screened for antioxidant and anti-inflammatory activity.

Reaction Scheme



R = 3-Br-4-OCH_3; 2,5-$(OCH_3)_2$; 4-OCH_3-3-NO_2; 3-Cl-4-OCH_3; 2-Cl-4-F; 2-Cl-5-NO_2; 2-Cl-5-CF_3; 3-Br-4-F; 3-phenoxy

CHAPTER V: Synthesis, Molecular docking and Biological Activity Studies of Novel Sulfathiazole Derivatives.

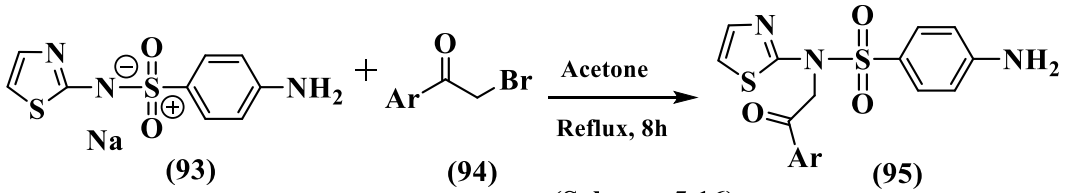
Thiazoles ring systems have been part of naturally occurring compounds such as thiamine and thiamine pyrophosphate, Sulfathiazoles are considered as the first efficient antibacterial agents serving medicinal need since their discovery[113]. They are synthesized by replacing one amidic hydrogen of sulfanilamide by a thiazole ring[114,115]. Thiazoles and sulfathiazole derivatives are well known for their wide spread pharmacological potential such as antimicrobial[14,116,117], antiviral[118], antituberculosis[119], anti-inflammatory[120], anticancer[9], 12-Lipoxygenase[121], antioxidant[122] agents. In addition, these compounds are also found as core motifs in solar cells[123], fluorocent dyes[20], transistors[19], corrosion inhibitors[124], voltage-gated sodium channel[125]. Enthused by the biological importance of Sulfathiazole drug and its adverse effects, we synthesized novel Sulfathiazole derivatives and screened them for various biological activities.

Materials and Method

To a dissolved solution of sodium salt of sulfathiazole **(93)** in acetone added various substituted phenacyl halides **(94)**. The mixture was stirred well and refluxed for about 8h. After the completion of reaction, reaction mixture was poured into crushed ice. Solid separated **(95a-j)** was collected. The reaction scheme is depicted in Scheme-5.16. Newly synthesized compounds were characterized by

^{1}H NMR, ^{13}C NMR and Mass spectral studies. All the synthesized compounds were screened for antimicrobial, antioxidant, anti-inflammatory activity. Antidiabetic activity was studied for compounds 3h, 3i and 3j.

Reaction Scheme



(93) **(94)** **(95)**

(Scheme-5.16)

Ar = 4-CH_3-Ph; 4-NO_2-Ph; 4-Cl-Ph; 4-Br-Ph; Ph;, 4-F-Ph; 4-OCH_3-Ph; biphenyl; naphthalene; 4-OH-3-$CONH_2$-Ph

References:

1. A. Al-Mulla, *Der Pharma Chem.*, 2017, **9**, 141–147.
2. M. S. Saini, A. Kumar, J. Dwivedi and R. Singh, *Int. J. Pharma Sci. Res.*, 2013, **4**, 66–77.
3. A. Pragi, A. Varun, H. . Lamba and D. Wadha, *Int. J. Pharm. Sci. Res.*, 2012, **15**, 421–429.
4. D. K. Dalvie, A. S. Kalgutkar, S. C. Khojasteh-bakht, R. S. Obach and J. P. O'donnel, *Chem.Res. Toxicol.*, 2002, **15**, 269–299.
5. H. Tunel, M. Er, H. Alici, A. Onaran, T. Karakurt and H. Tahtaci, *J. Heterocycl. Chem.*, 2021, **58**, 1321–1343.
6. S. Malladi, R. V. Nadh, K. S. Babu and P. S. Babu, *Beni-Suef Univ. J. Basic Appl. Sci.*, 2017, **6**, 345–353.
7. J. M. Padrón, D. Tejedor, A. Santos-Expósito, F. García-Tellado, V. S. Martín and J. Villar, *Bioorganic Med. Chem. Lett.*, 2005, **15**, 2487–2490.
8. S. M. Constantin, F. G. Lupascu, M. Apotrosoaei, A. V. Focsa, I. M. Vasincu, L. G. Confederat, G. Dimitriu, C. E. Lupusoru, S. Routier, F. Buron and L. Profire, *J. Drug Deliv. Sci. Technol.*, 2020, **60**, 102091.
9. P. C. Sharma, K. K. Bansal, A. Sharma, D. Sharma and A. Deep, *Eur. J. Med. Chem.*, 2020, **188**, 112016.
10. S. M. El-Moghazy, F. F. Barsoum, H. M. Abdel-Rahman and A. A. Marzouk, *Med. Chem. Res.*, 2012, **21**, 1722–1733.
11. A. A. Abdelhamid, H. A. Salah and A. A. Marzouk, *J. Heterocycl. Chem.*, 2020, **57**, 676–685.
12. D. J. Fu, P. Li, B. W. Wu, X. X. Cui, C. Bin Zhao and S. Y. Zhang, *Eur. J. Med. Chem.*, 2019, **165**, 309–322.
13. A. A. Bekhit, A. M. M. Hassan, H. A. Abd El Razik, M. M. M. El-Miligy, E. J. El-Agroudy and

A. E. D. A. Bekhit, *Eur. J. Med. Chem.*, 2015, **94**, 30–44.

14. S. Mondal, S. M. Mandal, T. K. Mondal and C. Sinha, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.*, 2015, **150**, 268–279.
15. H. Fuji, E. Urano, Y. Futahashi, M. Hamatake, J. Tatsumi, T. Hoshino, Y. Morikawa, N. Yamamoto and J. Komano, *J. Med. Chem.*, 2009, **52**, 1380–1387.
16. A. P. Nikalje, A. Ansari, S. Bari and V. Ugale, *Arch. Pharm. (Weinheim).*, 2015, **348**, 433–445.
17. D. Aydin, E. Karakilic, S. Karakurt and A. Baran, *Spectrochim. Acta - Part A Mol. Biomol. Spectrosc.*, 2020, **238**, 118431.
18. A. Doner, E. A. Sahin, G. Kardas and O. Serindag, *Corros. Sci.*, 2013, **66**, 278–284.
19. S. Ando, R. Murakami, J. I. Nishida, H. Tada, Y. Inoue, S. Tokito and Y. Yamashita, *J. Am. Chem. Soc.*, 2005, **127**, 14996–14997.
20. J. Nygren, N. Svanvik and M. Kubista, *Biopolymers*, 1998, **46**, 39–51.
21. J. Zhuang and S. Ma, *ChemMedChem*, 2020, **15**, 1875–1886.
22. B. Tozkoparan, M. Ertan, P. Kelicen and R. Demirdamar, *Farmaco*, 1999, **54**, 588–593.
23. A. Mahapatra, T. Prasad and T. Sharma,*Futur. J. Pharm. Sci*., 2021, **7**, 123.
24. J. N. Lalpara, M. D. Vachhani, S. D. Hadiyal, S. Goswami and G. G. Dubal, *Russ. J. Org. Chem.*, 2021, **57**, 241–246.
25. M. M. M. Ramiz, W. A. El-sayed, E. Hagag and Adel A. H. abdel-rahman, *J. Heterocycl. Chem.*, 2011, **48**, 1028–1038.
26. A. E. G. E. Amr, H. H. Sayed and M. M. Abdulla, *Arch. Pharm. (Weinheim).*, 2005, **338**, 433–440.
27. H. Wang, A. Wang, J. Gu, L. Fu, K. Lv, C. Ma, Z. Tao, B. Wang, M. Liu, H. Guo and Y. Lu, *Eur. J. Med. Chem.*, 2019, **165**, 11–17.
28. I. A. M. Radini, T. M. Y. Elsheikh, E. M. El-Telbani and R. E. Khidre, *Molecules*, 2016, **21**, 10–21.
29. R. P. Modh, E. De Clercq, C. Pannecouque and K. H. Chikhalia, *J. Enzyme Inhib. Med. Chem.*, 2014, **29**, 100–108.
30. M. Mao, X. Zhang, B. Zhu, J. Wang, G. Wu, Y. Yin and Q. Song, *Dye. Pigment.*, 2016, **124**, 72–81.
31. Z. Zhang, J. Xie, H. Wang, B. Shen, J. Zhang, J. Hao, J. Cao and Z. Wang, *Dye. Pigment.*, 2016, **125**, 299–308.
32. D. R. Patel and K. C. Patel, *Fibers Polym.*, 2010, **11**, 537–544.
33. I. S. Park, H. Komiyama and T. Yasuda, *Chem. Sci.*, 2017, **8**, 953–960.
34. Y. Lei, T.-Z. Li, C. Fu, X.-L. Guan and Y. Tan,*J. Chil. Chem. Soc*., 2015, **60**, 2961–2965.
35. N. Kumar and L. S. Chauhan, *Int. J. Pharm. Clin. Res*., 2015, **7**, 154–161.

36. V. Ferraresi-Curotto, G. A. Echeverría, O. E. Piro, R. Pis-Diez and A. C. González-Baró, *J. Mol. Struct.*, 2017, **1133**, 436–447.
37. N. S. El-Din and A. Barseem, *J. Appl. Pharm. Sci.*, 2016, **6**, 075–083.
38. A. Kajal, S. Bala, N. Sharma, S. Kamboj and V. Saini, *Int. J. Med. Chem.*, 2014, **2014**, 1–11.
39. M. Taha, N. H. Ismail, H. M. Zaki, A. Wadood, E. H. Anouar, S. Imran, B. M. Yamin, F. Rahim, M. Ali and K. M. Khan, *Bioorg. Chem.*, 2017, **75**, 235–241.
40. P. Nefisath, J. P. Dasappa, B. Haripriya, D. Chopra, K. N. Venugopala, P. K. Deb, R. M. Gleiser, V. Mohanlall, R. Maharaj, Shashiprabha and V.Poojary, *J. Mol. Struct.*, 2021, **1236**, 130305.
41. T. Govindasami, A. Pandey, N. Palanivelu and A. Pandey, *Int. J. Org. Chem.*, 2011, **01**, 71–77.
42. G. L. Backes, D. M. Neumann and B. S. Jursic, *Bioorganic Med. Chem.*, 2014, **22**, 4629–4636.
43. B. B. Casanova, M. N. Muniz, T. De Oliveira, L. F. De Oliveira, M. M. Machado, A. M. Fuentefria, G. Gosmann and S. C. B. Gnoatto, *Molecules*, 2015, **20**, 9229–9241.
44. H. S. Kareem, A. Ariffin, N. Nordin, T. Heidelberg, A. Abdul-Aziz, K. W. Kong and W. A. Yehye, *Eur. J. Med. Chem.*, 2015, **103**, 497–505.
45. V. Onnis, M. T. Cocco, R. Fadda and C. Congiu, *Bioorganic Med. Chem.*, 2009, **17**, 6158–6165.
46. V. Kamat, R. Santosh, B. Poojary, S. P. Nayak, B. K. Kumar, M. Sankaranarayanan, Faheem, S. Khanapure, D. A. Barretto and S. K. Vootla, *ACS Omega*, 2020, **5**, 25228–25239.
47. P. A. Castelino, J. P. Dasappa, P. Naik, S. C. Kodandoor, and A. Kumari, *Indian J. Appl. Res.*, 2014,**4**, 25–31.
48. S. A. A. Noma, M. Erzengin, T. Tunc and S. Balcıoglu, *J. Mol. Struct.*,**1205**, 2020, 127550.
49. R. Sreenivasulu, K. T. Reddy, P. Sujitha, C. G. Kumar and R. R. Raju, *Bioorganic Med. Chem.*, 2019, **27**, 1043–1055.
50. N. Raghav and M. Singh, *Bioorganic Med. Chem.*, 2014, **22**, 4233–4245.
51. U. Ashiq, R. A. Jamal, M. N. Tahir, S. Yousuf and I. U. Khan, *Acta Crystallogr. Sect. E Struct. Reports Online*, 2009, **65**, o1551–o1551.
52. V. B. Tatipamula and G. S. Vedula, *J. Serbian Chem. Soc.*, 2019, **84**, 555–562.
53. J. Pisk, I. Dilovic, T. Hrenar, D. Cvijanovic, G. Pavlovic and V. Vrdoljak, *RSC Adv.*, 2020, **10**, 38566–38577.
54. P. anastas and N. Eghbali, *Chem. Soc. Rev.*, 2010, **39**, 301-312.
55. Y. Hu, C. Y. Li, X. M. Wang, Y. H. Yang and H. L. Zhu, *Chem. Rev.*, 2014, **114**, 5572–5610.
56. S. S. Kadam and G. M. Nazeruddin,*World J. Pharm. Res*., 2016,**5**, 1456-1466.
57 .E. Palaska, G. Sahin, P. Kelicen, N. T. Durlu and G.Altinok,*Farmaco*, 2002,**57**, 101–107.
58 .V. A. Obakachi, B. Kushwaha, N. D. Kushwaha, S. Mokoena, A. M. Ganai, T. K. Pathan, W. E. van Zyl and R. Karpoormath, *J. Sulfur Chem.*, 2021, **42**, 670–691.
59 .P. A. Datar and T. A. Deokule,*Med. Chem. (Los. Angeles).*, 2014, **4**, 390–399.

60. C. Man, Y. Wang, W. Li, D. Kong, J. Yao, H. Grothe, Z. Cui, X. Wang and C. Dong, *Prog. Org. Coatings*, 2021, **159**, 106441.
61. L. Biniek, I. Bulut, P. Lévêque, T. Heiser and N. Leclerc, *Tetrahedron Lett.*, 2011, **52**, 1811–1814.
62. M. Khalid, A. Ali, S. Haq, M. N. Tahir, J. Iqbal, A. A. C. Braga, M. Ashfaq and S. U. H. Akhtar, *J. Mol. Struct.*, 2021, **1224**, 129308.
63. A. L. Khandazhinskaya, L. A. Alexandrova, E. S. Matyugina, P. N. Solyev, O. V. Efremenkova, K. W. Buckheit, M. Wilkinson, R. W. Buckheit, L. N. Chernousova, T. G. Smirnova, S. N. Andreevskaya, O. G. Leonova, V. I. Popenko, S. N. Kochetkov and K. L. Seley-Radtke, *Molecules*, 2018, **23**, 3069.
64. F. Panahi, R. Yousefi, M. H. Mehraban and A. Khalafi-Nezhad, *Carbohydr. Res.*, 2013, **380**, 81–91.
65. S. N. Sirakanyan, E. K. Akopyan, R. G. Paronikyan, A. G. Akopyan and A. A. Ovakimyan, *Pharm. Chem. J.*, 2016, **50**, 296–300.
66. E. V. Verbitskiy, A. S. Steparuk, E. F. Zhilina, V. V. Emets, V. A. Grinberg, E. V. Krivogina, S. A. Kozyukhin, E. V. Belova, P. I. Lazarenko, G. L. Rusinov, A. R. Tameev, J. M. Nunzi and V. N. Charushin, *Electron. Mater.*, 2021, **2**, 142–153.
67. L. P. Duan, Q. F. Zhao and H. B. Zhang, *Arab. J. Chem.*, 2010, **3**, 225–228.
68. N. S. El-Sayed, E. R. El-Bendary, S. M. El-Ashry and M. M. El-Kerdawy, *Eur. J. Med. Chem.*, 2011, **46**, 3714–3720.
69. T. M. Salimov, M. A. Kukaniev, I. T. Sattorov, D. M. Osimov,*Pharm. Chem. J.*,2005,**39**, 28–29.
70. F. L. Chubb and J. Nissenbum, *Can. J. Chem.*, 1959, **37**, 1121–1123.
71. B. Zhao, Y. Xu, Q. G. Deng, Z. Liu, L. Y. Wang and Y. Gao, *Tetrahedron Lett.*, 2014, **55**, 4521–4524.
72. N. Kerru, L. Gummidi, S. N. Maddila, S. V. H. S. Bhaskaruni, S. Maddila and S. B. Jonnalagadda, *RSC Adv.*, 2020, **10**, 19803–19810.
73. M. Dagli, M. Er, T. Karakurt, A. Onaran, H. Alici and H. Tahtaci, *ChemistrySelect*, 2020, **5**, 11753–11763.
74. A. Bhatnagar, P. K. Sharma and N. Kumar, *Int. J. PharmTech Res.*, 2011, **3**, 268–282.
75. P. Sharma, C. Larosa, J. Antwi, R. Govindarajan and K. A. Werbovetz, *Molecules*, 2021, **26**, 4213.
76. P. A. Channar, A. Saeed, F. A. Larik, M. Bolte and M. F. Erben, *J. Mol. Struct.*, 2019, **1179**, 11–17.
77. M. Er, H. Tahtaci, T. Karakurt and A. Onaran, *J. Heterocycl. Chem.*, 2019, **56**, 2555–2570.

78. S. G. Alegaon and K. R. Alagawadi,*Eur. J. Chem*., 2011, **2**, 2–7.
79. V. Bhardwaj, M. N. Noolvi, S. Jalhan and H. M. Patel, *J. Saudi Chem. Soc.*, 2016, **20**, S406–S410.
80. R. S. Lamani, N. S. Shetty, R. R. Kamble and I. A. M. Khazi, *Eur. J. Med. Chem.*, 2009, **44**, 2828–2833.
81. V. B. Jadhav, M. V. Kulkarni, V. P. Rasal, S. S. Biradar and M. D. Vinay, *Eur. J. Med. Chem.*, 2008, **43**, 1721–1729.
82. S. S. Karki, K. Panjamurthy, S. Kumar, M. Nambiar, S. A. Ramareddy, K. K. Chiruvella and S. C. Raghavan, *Eur. J. Med. Chem.*, 2011, **46**, 2109–2116.
83. B. Chakrapani, V. Ramesh, G. Pourna Chander Rao, D. Ramachandran, T. Madhukar Reddy, A. Kalyan Chakravarthy and G. Sridhar, *Russ. J. Gen. Chem.*, 2018, **88**, 1020–1024.
84. B. Choodamani, K. G. Cano Hernandez, S. Kumar, A. M. Tony, A. Y. Schiaffino Bustamante, R. J. Aguilera, D. Schols, C. Gopi Mohan and S. S. Karki, *Chem. Biodivers.*, 2021, **18**, e2000800.
85. R. Kumar, S. Bua, S. Ram, S. Del Prete, C. Capasso, C. T. Supuran and P. K. Sharma, *Bioorganic Med. Chem.*, 2017, **25**, 1286–1293.
86. H. M. Patel, M. N. Noolvi, A. Goyal and B. S. Thippeswamy, *Eur. J. Med. Chem.*, 2013, **65**, 119–133.
87. M. M. Ishankhodzhaeva, S. A. Kadyrova, M. D. Surazhskaya, N. A. Parpiev and P. A. Koz'min, *Russ. J. Org. Chem.*, 2001, **37**, 721–723.
88. H. M. Patel, M. N. Noolvi, N. S. Sethi, A. K. Gadad and S. S. Cameotra, *Arab. J. Chem.*, 2017, **10**, S996–S1002.
89. M. W. Drăgan, C. D. Stan, A. Pânzariu, A. Jităreanu and L. Profire, *Farmacia*, 2015, **63**, 150–154.
90. D. Havrylyuk, B. Zimenkovsky, O. Vasylenko, L. Zaprutko, A. Gzella and R. Lesyk, *Eur. J. Med. Chem.*, 2009, **44**, 1396–1404.
91. N. O. Mahmoodi, M. Mohammadi Zeydi, E. Biazar and Z. Kazeminejad, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2017, **192**, 344–350.
92. R. Ranga, V. Sharma and V. Kumar, *Med. Chem. Res.*, 2013, **22**, 1538–1548.
93. G. H. Gong, D. Wang, J. F. Zhang, C. X. Wei and Z. S. Quan, *Drug Res.(Stuttg).*, 2014, **64**, 5-9.
94. V. Murugesan, Y. S. Prabhakar and S. B. Katti, *J. Mol. Graph. Model.*, 2009, **27**, 735–743.
95. R. K. Rawal, Y. S. Prabhakar, S. B. Katti and E. De Clercq, *Bioorganic Med. Chem.*, 2005, **13**, 6771–6776.
96. G. Meng, M. Zheng, M. Wang, J. Tong, W. Ge, J. Zhang, A. Zheng, J. Li, L. Gao and J. Li, *Eur.*

J. Med. Chem., 2016, **122**, 756–769.

97. L. Gummidi, N. Kerru, O. Ebenezer, P. Awolade, O. Sanni, M. S. Islam and P. Singh, *Bioorg. Chem.*, 2021, **115**, 105210.
98. B. Pan, R. Z. Huang, S. Q. Han, D. Qu, M. L. Zhu, P. Wei and H. J. Ying, *Bioorganic Med. Chem. Lett.*, 2010, **20**, 2461–2464.
99. M. Apotrosoaei, I. M. Vasincu, M. Dragan, F. Buron, S. Routier and L. Profire, *Molecules*, 2014, **19**, 13824–13847.
100. S. Constantin, F. G. Lupascu, M. Apotrosoaei, I. M. Vasincu, D. Lupascu, F. Buron, S. Routier and L. Profire, *Chem. Cent. J.*, 2017, **11**, 1–13.
101. P. Muralidharan and G. Subramaniam, *Pharmacol. Toxicol. Biomed. Reports*, 2017, **3**, 35–38.
102. R. Ottanaa, E. Mazzon, L. Dugo, F. Monforte, R. Maccari, L. Sautebin, G. De Luca, M. G. Vigorita, S. Alcaro, F. Ortuso, A. P. Caputi and S. Cuzzocrea, *Eur. J. Pharmacol.*, 2002, **448**, 71–80.
103. S. P. Khathi, B. Chandrasekaran, S. Karunanidhi, C. L. Tham, F. Kozielski, N. Sayyad and R. Karpoormath, *Bioorganic Med. Chem. Lett.*, 2018, **28**, 3489.
104. E. Tatar, I. Kucukguzel, E. De Clercq, R. Krishnan and N. Kaushik-Basu, *Marmara Pharm. J.*, 2012, **16**, 181–193.
105. T. Previtera, M. Vigorita, M. Basile, F. Orsini, F. Benetollo and G. Bombieri, *Eur. J. Med. Chem.*, 1994, **29**, 317–324.
106. H. Ayalew, G. Reda, T. Gashaw, N. Babu and R. K. Upadhyay, *ISRN Org. Chem.*, 2014, **2014**, 1–8.
107. R. Abdizadeh, F. Hadizadeh and T. Abdizadeh, *Struct. Chem.*, 2020, **31**, 1149–1182.
108. D. D. Subhedar, M. H. Shaikh, M. A. Arkile, A. Yeware, D. Sarkar and B. B. Shingate, *Bioorganic Med. Chem. Lett.*, 2016, **26**, 1704–1708.
109. S. Raza, S. P. Srivastava, D. S. Srivastava, A. K. Srivastava, W. Haq and S. B. Katti,*Eur. J. Med. Chem.*, 2013,**63**, 611–620.
110. C. M. Bhalgat, P. V. Darda, K. G. Bothara, S. V. Bhandari, J. Gandhi and B. Ramesh, *Eur. J. Med. Chem.*, 2014, **76**, 580–588.
111. T. J. Reilly, *J. Chem. Educ.*, 1999, **76**, 1557.
112. M. Bhat, B. Poojary, B. S. Kalal, P. M. Gurubasavaraja Swamy, S. Kabilan, V. Kumar, N. Shruthi, S. A. Alias Anand and V. R. Pai, *Future Med. Chem.*, 2018, **10**, 1017–1036.
113. H. Mohammadi and H. R. Shaterian, *Res. Chem. Intermed.*, 2020, **46**, 1109–1125.
114. M. C. Bordier, E. A. Navarro, R. Cámpora, M. C. Navarro and M. I. Gómez, *J. Chil. Chem. Soc.*, 2014, **59**, 2315–2318.
115. D. Das, P. Sikdar and M. Bairagi, *Eur. J. Med. Chem.*, 2016, **109**, 89–98.

116. K. Liaras, A. Geronikaki, J. Glamočlija, A. Ćirić and M. Soković, *Bioorganic Med. Chem.*, 2011, **19**, 3135–3140.
117. N. C. Desai, V. V. Joshi, K. M. Rajpara, H. V. Vaghani and H. M. Satodiya, *J. Fluor. Chem.*, 2012, **142**, 67–78.
118. I. P. Singh, S. Gupta and S. Kumar, *Med. Chem. (Los. Angeles).*, 2020, **16**, 4–23.
119. M. R. Shiradkar, K. K. Murahari, H. R. Gangadasu, T. Suresh, C. A. Kalyan, D. Panchal, R. Kaur, P. Burange, J. Ghogare, V. Mokale and M. Raut, *Bioorganic Med. Chem.*, 2007, **15**, 3997–4008.
120. M. H. M. Helal, M. A. Salem, M. S. A. El-Gaby and M. Aljahdali, *Eur. J. Med. Chem.*, 2013, **65**, 517–526.
121. D. K. Luci, J. B. Jameson, A. Yasgar, G. Diaz, N. Joshi, A. Kantz, K. Markham, S. Perry, N. Kuhn, J. Yeung, E. H. Kerns, L. Schultz, M. Holinstat, J. L. Nadler, D. A. Taylor-Fishwick, A. Jadhav, A. Simeonov, T. R. Holman and D. J. Maloney, *J. Med. Chem.*, 2014, **57**, 495–506.
122. V. Jaishree, N. Ramdas, J. Sachin and B. Ramesh, *J. Saudi Chem. Soc.*, 2012, **16**, 371–376.
123. D. Zhu, X. Bao, Q. Zhu, C. Gu, M. Qiu, S. Wen, J. Wang, B. Shahid and R. Yang, *Energy Environ. Sci.*, 2017, **10**, 614–620.
124. K. F. Khaled and M. A. Amin, *Corros. Sci.*, 2009, **51**, 1964–1975.
125. D. S. La, E. A. Peterson, C. Bode, A. A. Boezio, H. Bregman, M. Y. Chu-Moyer, J. Coats, E. F. DiMauro, T. A. Dineen, B. Du, H. Gao, R. Graceffa, H. Gunaydin, A. Guzman-Perez, R. Fremeau, X. Huang, C. Ilch, T. J. Kornecook, C. Kreiman, J. Ligutti, M. H. Jasmine Lin, J. S. McDermott, I. Marx, D. J. Matson, S. I. McDonough, B. D. Moyer, H. Nho Nguyen, K. Taborn, V. Yu and M. M. Weiss, *Bioorganic Med. Chem. Lett.*, 2017, **27**, 3477–3485.

Papers Communicated

Anticancer, antimicrobial activities and nonlinear optical property studies of some aroylhydrazones, Rajatha Mudya[a], Sukumar Kotyan[a] , Ravindra R. Kamble[b], Praveen Kumar[b], K. Sharath Chandra[c], Prashantha Naik[c], Guruprasad Kalathur[d], Jagadeesh Prasad Dasappa[a]*

Communicated to Journal of Molecular Structure, Manuscript No. MOLSTRUC-D-24-04803R1(under review)

Conference Presentations:

1. Participated and presented a paper on ‘Synthesis of some novel hydrazones and antibacterial activity studies’, in National Seminar on Lab to clinic: Approaches and challenges in drug discovery, design and delivery’ organised by the Deptartment of Bioscience, Mangalore University, Mangalagangotri and Royal Society of Chemistry (London) India Deccan Local Section National from23rd - 24th February 2018.
2. Participated and presented a paper on ‘Synthesis and anticancer activity of some novel hydrazone derivatives’, in two days national conference on ‘Impact of chemistry and biology to the society and industry (ICBSI)’ held at Kuvempu University, Jnana Sahyadri, from 20th - 21st May 2022.
3. Participated and presented a paper on ‘Antioxidant and Anti-inflammatory Activity Studies of Some Novel Imidazothiadiazole Derivatives’, in two days national conference on ‘Advanced Materials for Chemical and Biological Applications (NCAMCBA)’ held at Sri Dharmasthala Manjunatheshwara Post Graduation Centre, Ujire, from 6th-7th March 2024.

Signature of the Student **Signature of the Guide**